REMARKS/ARGUMENTS

In the specification, the abstract of the application on a separate sheet is enclosed in the appendix as requested.

Claims 1-33 are pending. Claims 1-32 have been examined. No claims have been amended.

1. Rejection Under 35 U.S.C. § 101

Claims 1-32 were rejected under 35 U.S.C. § 101, as allegedly having no apparent or disclosed patentable utility. Applicants respectfully traverse.

Applicants were directed to the Utility Examination Guidelines, Federal Register, Vol. 66, No. 4, pages 1092-1099, Friday January 5, 2001. Under the Guidelines, the present application has a well established utility.

1a. The homology-based assertions of utility

The USPTO explicitly declined to adopt the suggestions to adopt a *per se* rule rejecting homology-based assertions of utility, and required that each application must be judged on its own merits. When a patent application claiming a nucleic acid asserts a specific, substantial, and credible utility, and bases the assertion upon homology to existing nucleic acids or proteins having an accepted utility, the asserted utility must be accepted by the examiner unless the Office has sufficient evidence or sound scientific reasoning to rebut such an assertion. (Federal Register, Vol. 66, No. 4, pages 1096)

The Examiner questioned the homology-based assertions of utility, citing some pitfalls of homology-based prediction of protein function described by *Doerks* et al, 1998, *Doerks* et al, *Brenner*, and *Bork*. From the references, however, it could not be concluded that homology-based assertions of utility should not be adopted. Indeed, one of skill in the art would improve the homology-based assertions of utility by realizing and avoiding the pitfalls. Thus, the Examiner did not provide scientific evidence that homology-based assertions of utility are inherently unbelievable or involve implausible scientific principles.

Brenner v. Manson (148 USPQ 689 (Sup. Ct., 1966)), which is cited by the Examiner, set out the utility requirements: specific, substantial, and credible utility. As discussed herein, the present application has met all the utility requirements. However, *Brenner*, rejecting the structure-homologue-based prediction of utility based on for a **steroid**, cannot be overstretched to reject the sequence-homology-based assertions of utility of a **protein**. One of skill in the art would know the great structural and functional differences between steroid and protein. Indeed, *Brenner*'s rejection of the prediction of utility is predicated on the specific characteristics of steroid compounds. In *Brenner*, for instance, even the respondent himself recognized that the presumption that adjacent homologues have the same utility has been challenged in the steroid field because of "a greater known unpredictability of compounds in that field." In contrast, as discussed above, there is no such an unpredictability in the current field of sequence-homology-based prediction of functions for proteins.

HG51 of the present application is a novel member of GPCR family. The Examiner did not present any evidence to suggest that a specific, substantial, and credible utility of GPCR family may not be imputed to HG51.

1b. Orphan G-protein coupled receptors (GPCRs) have specific, substantial, and credible utilities

The Examiner stated that even if HG51 belongs to GPCR family, it is one of the orphan GPCRs. The Examiner argued that orphan GPCRs have no "real world" context use, because the ligands, functions, and associated diseases or conditions of them are unknown.

An orphan GPCR can be used in drug discovery even before its ligands, functions, and associated diseases or conditions are determined. GPCRs have a proven history of being excellent therapeutic targets. Consequently, orphan GPCRs have great potential for pioneer drug industry. Stadel et al described the strategies for converting orphan GPCRs into therapeutic targets. (TiPS, p430-437, November 1997 (Vol. 18)) Orphan GPCRs, including HG51, can be used as candidates for therapeutic targets for a drug discovery approach called "reverse molecular pharmacology". Such a use of orphan GPCRs is a well established use that is specific, substantial and credible. The use is specific because the "reverse molecular pharmacology" is

specifically designed for orphan GPCRs. This use is substantial because it is a "real world" context of use.

1c. HG51 has specific, substantial, and credible utilities

When a class of proteins is defined such that the members share a specific, substantial, and credible utility, the reasonable assignment of a new protein to the class of sufficiently conserved proteins would impute the same specific, substantial, and credible utility to the assigned protein. (Federal Register, Vol. 66, No. 4, pages 1096) Thus, the drug discovery use of orphan GPCRs should be imputed to HG51.

In addition, the drug discovery use of HG51 is also disclosed in the present application. (for example, p23, line 19 – p24, line 7 describes screening compounds to identify potential pharmaceuticals that specifically interact with HG51)

Moreover, the studies disclosed in the present application provided leads for the ligands and functions, and associated diseases or conditions of HG51. For example, HG51 contains a lysine residue that is critical form Schiff base in opsin, suggesting that the ligand may be fatty-acid-like molecule. The HG51 is expressed in a wide variety of tissue, it should have important functions in metabolism. (p4, lines 4-16 of the specification) The information would facilitate the drug discovery using HG51.

Hence, HG51 can be used in drug discovery as other orphan GPCRs, although its ligands, functions, and associated diseases or conditions are not exactly known yet. With such a specific, substantial, and credible utility of HG51, the present application met all the utility requirements.

Moreover, the utility of the diagnostic assays to detect HG51, which is credible and substantial according to the Examiner, is also specific. The antibodies or polynucleotide probes are designed to specifically recognize the HG51 polypeptide or HG51 mRNA, rather than any polypeptide or any polynucleotide. The hybridization probes recognizing HG51 mRNA can be designed from the HG51 polynucleotide sequence, rather than any polynucleotide sequence.

2. Rejection Under 35 U.S.C. § 112, 1st paragraph

2a. The enablement rejection

Claims 26-32 were rejected under 35 U.S.C. § 112, as allegedly not reasonably providing enablement for the fragments, and mutants of HG51. Applicants respectfully traverse.

According to the present invention, HG51 is a novel human G-protein coupled receptor having an amino sequence disclosed in Figure 2 and set forth as SEQ ID NO:2 (p4, lines 4-6 of the specification). It is the biologically active fragments and/or mutants of HG51 that include amino acid substitutions, deletions, additions, and truncations of HG51 (p5, lines 15-20 of the specification). Claims 26-32 recite "HG51" rather than "biologically active fragments and/or mutants of HG51".

Claims 6-8, and 17-19 were rejected under 35 U.S.C. § 112, as allegedly not reasonably providing enablement for *in vivo* transfection. Applicants respectfully traverse.

Eck & Wilson, which was cited by the Examiner, discussed the problems that limit clinically efficacious gene therapy (page 81, col. 2, para. 1 to page 82, col. 1 para. 2). However, *Eck & Wilson*, did not say the problems would limit the expression of a recombinant protein in cells within a host animal. After all, such an expression itself is much easier than clinically efficacious gene therapy.

In addition, one of skill in the art would know that the expression of a recombinant protein in cells within a host animal can also be achieved with approaches other than gene therapy, such as the techniques of transgenic animals.

2b. The written description rejection

Claims 26-32 were rejected under 35 U.S.C. § 112, as allegedly lacking written description. Applicants respectfully traverse.

According to the present invention, HG51 is a novel human G-protein coupled receptor having an amino sequence disclosed in Figure 2 and set forth as SEQ ID NO:2 (p4, lines 4-6 of the specification). It is the biologically active fragments and/or mutants of HG51 that include

amino acid substitutions, deletions, additions, and truncations of HG51 (p5, lines 15-20 of the specification). Claims 26-32 recite "HG51" rather than "biologically active fragments and/or mutants of HG51".

3. Rejection Under 35 U.S.C. § 112, 2nd paragraph

Claims 25-32 were rejected under 35 U.S.C. § 112, as allegedly being indefinite. Applicants respectfully traverse.

The term "effect" recited in claim 25 is definite. The present application provides guidance in the specification as to what effect is to be measured. (See, e.g., p22, line 30 – p24, line 35)

The term "potential" recited in claim 26 is definite. Claim 26 is directed to a method for determining whether a substance is a potential agonist or antagonist of HG51. The term "potential" is recited to indicate further steps, in addition to the recited steps, may be or may be not needed to verify the tested substance as an agonist or antagonist of HG51. Claim 26 recites "comprising", indicating that further steps can be added, such as further verifying steps or further chemical modifications. Such an openness of a claim should not make the claim indefinite.

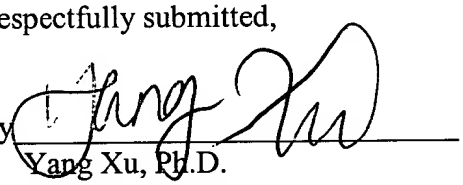
The term "HG51" recited in claims 26-32 is definite. According to the present invention, HG51 is a novel human G-protein coupled receptor having an amino sequence disclosed in Figure 2 and set forth as SEQ ID NO:2 (p4, lines 4-6 of the specification).

Accordingly, the Applicants respectfully request that the examiner reconsider the decision and withdraw the restriction requirement.

It is believed that no additional fee is required with this submission. However, should an additional fee be required, the Commissioner is hereby authorized to charge the fee to Deposit Account No. 13-2755.

Allowance of claims 1-33 is earnestly solicited.

Respectfully submitted,

By 

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